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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/072,010 | 10/25/2001 | Jonathan W. Nyce | EPI-00312 | 5176 |

27194 7590 03/09/2004

HOWREY SIMON ARNOLD & WHITE, LLP
BOX 34
301 RAVENSWOOD AVE.
MENLO PARK, CA 94025

| EXAMINER | |
|---|---|
| JIANG, SHAOJIA A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/072,010 | NYCE, JONATHAN W. | |
| | Examiner | Art Unit | |
| | Shaojia A Jiang | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *160-186* is/are pending in the application.

4a) Of the above claim(s) *166-186* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *160-165* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 19, 2003 has been entered.

This Office Action is a response to Applicant's request for continued examination (RCE) filed December 19, 2003, and amendment and response to the Final Office Action (mailed April 23, 2003), filed December 19, 2003 wherein claims 1-159 are cancelled, and claims 160-186 are newly submitted. Currently, claims 160-186 are pending in this application.

It is noted that the newly claims 167-186 are drawn to a method of treatment of prphylaxis of bronchoconstriction, lung inflammation, lung allergy, or asthma, comprising administering to a subject in need of such treatment or prophylaxis of a therapeutically effective amount of the pharmaceutical composition in claim 160 and an in vivo method of preventing or treating a disorder or condition associated with abnormal levels of adenosine and other conditions herein employing the composition of claim 160, that are independent and distinct from the invention elected originally by Applicant's agent, Dr. Viviana Amzel on April 29, 2002, to prosecute the invention of Group I, claims 80-127, which is entirely directed to a pharmaceutical composition

herein and a kit comprising compounds having the chemical formula (I) and/or (II) (see the previous Office Action including Restriction Requirement mailed May 7, 2002). As recorded in the previous Office Action May 7, 2002, the original Claims 128-158 drawn to an in vivo method of preventing or treating a disorder or condition associated with abnormal levels of adenosine and other conditions herein employing compounds having the chemical formula (I) and (II), have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Further, the new claim 166 is directed to the combination of the compound of formula (I) and folinic acid that is also independent and distinct from the invention elected originally by Applicant's agent, Dr. Viviana Amzel on April 29, 2002, to prosecute the invention of Group I, claims 80-127, which is directed to a pharmaceutical composition herein and a kit comprising compounds having the chemical formula (I) alone or combining with ubiquinone having the formula (II) only. Thus, these two compositions between claim 166 and the original claims 80-127 have different modes of operation and different functions.

Applicant is requested to note that according to MPEP § 819, the general policy of the Office is not to permit the applicant to shift to claiming another invention after **an election is once made and/or an action given on the merits**.

Moreover, the applicant **cannot**, as a matter of right, file a request for continued examination (RCE) to obtain continued examination on the basis of claims that are independent and distinct from the claims previously claimed and examined (i.e.,

applicant cannot switch inventions by way of an RCE as a matter of right) (emphases added). See MPEP § 819.

Therefore, claims 166-186 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Regarding the method claims 167-186, as noted in MPEP § 804.01 (see below).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claims 160-165 are examined on the merits herein.

As recorded in the previous Office Action (may 7, 2002), this application is a division of 09/841,426 which is a continuation in part of Serial No. 09/488236 (now

patent 6,670,349) which is a continuation of 08/861,962 (patent 6,087,351) which is a divisional of 08/393,863 (patent 5,660,835).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 160-165 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for treatment of bronchoconstriction, lung inflammation, lung allergy, or asthma by administering the composition herein, does not reasonably provide enablement for the **prophylaxis** of bronchoconstriction, lung inflammation, lung allergy, or asthma employing the composition in claim 160, and "prevent or counter" in claim 165.

The instant claims are drawn to the methods for the **prophylaxis** of or prevent bronchoconstriction, lung inflammation, lung allergy, or asthma in a human or animal subject. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The instant invention pertains to the method for the prophylaxis of or prevent bronchoconstriction, lung inflammation, lung allergy, or asthma in a human or animal subject.

The state of the prior art: The skilled artisan would view that the prophylaxis of or prevent bronchoconstriction, lung inflammation, lung allergy, or asthma in a human or animal subject totally, absolutely, or permanently, is highly unlikely, not even occurring at the first time.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or lack thereof in the art: The skilled artisan would view that the prophylaxis of or prevent bronchoconstriction, lung inflammation, lung allergy, or asthma in a human or animal subject totally, absolutely, or permanently is highly unpredictable, and not even occur at the first time is highly unpredictable.

The amount of direction or guidance presented and the presence or absence of working examples: In the instant case, **no** working examples are presented in the specification as filed showing how the prophylaxis of or how to prevent bronchoconstriction, lung inflammation, lung allergy, or asthma in a human or animal subject totally, absolutely, or permanently, not even occurring at the first time.

*Genentech*, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims and their combinations to be administered to a host employed in the claimed methods of the particular treatments herein, with no assurance of success.

Therefore, in view of the *Wands* factors, as discussed above, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art, Applicants fail to provide information sufficient to practice the claimed invention.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 165 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "the subject's tissue" renders the claim indefinite. The recitation " subject" is not clearly defined in the claims or specification. One of ordinary skill in the

art could interpret that the term "subject " would be a single cell, any biological system, an animal or a human. Thus, one of ordinary skill in the art could not interpret the metes and bounds of the patent protection desired as to what "subject" encompassed thereby.

Moreover Claims 165 recite the limitation "the subject's tissue". There is insufficient antecedent basis for this limitation in the claim since claim 160 does not recite any subject's tissue in the composition.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 160-164 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prendergast (4,956,355 of record) in view of Lieberman et al. (Pharmaceutical Dosage Forms, page 110).

Prendergast discloses that particular dehydroepiandrosterones (DHEA) herein are useful in a pharmaceutical composition or a pharmaceutical formulation of enteral, parental, injectable, topical or nasal inhalation administration (see col.5 lines 32-64, especially col.5 lines 49 and 63-64). See abstract, col.1 lines 36-57, col. 4-5 and claim 6. Prendergast also discloses the effective amounts of dehydroepiandrosterones in the

composition and other agents and pharmaceutically acceptable excipients within the instant claim in the compositions therein (col.5).

Prendergast does not expressly disclose the particular range of respirable particle size herein.

Lieberman et al. teaches that a skilled artisan in pharmaceutical science would clearly knowledge that the granulation, determination of size, or size reduction of a solid pharmaceutical formulation, e.g., in nasal inhalation formulation, have several benefits, for example, as taught in a text book "Pharmaceutical Dosage Forms" Tables, (Volume 2) Ed. by Herbert A. Lieberman, Leon Leachman, and Joseph B. Schwartz (1989) at page 110. Moreover, suitable particle sizes for nasal inhalation are generally known and available to one of ordinary skill in the art.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation, since particular dehydroepiandrosterones (DHEA) herein are known to be in a pharmaceutical composition for nasal inhalation administration based on Prendergast. According to conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in

the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 160 and 165 are rejected under 35 U.S.C. 103(a) as being unpatentable Nyce (5,527,789, of record) in view of Lieberman et al. (Pharmaceutical Dosage Forms, page 110).

Nyce discloses a pharmaceutical composition comprising the instant DHEA having the chemical formula (I) in a therapeutically effective amounts and the instant ubiquinone having the chemical formula (II) with n being from 1 to 12, 1 to 10, 6 to 10, or 10, in the therapeutically effective amounts, and a pharmaceutical carrier or diluent (see abstract, claims 13-19). Nyce also discloses the particular effective amounts of

DHEA, i.e., 1-3600 mg/kg, 5-1800 mg/kg, or 20-100 mg/kg (see col.6 lines 6-7); and the particular effective amounts of ubiquinone, i.e., 1-1200 mg/kg, 30-600 mg/kg, or 50-150 mg/kg (see col.5 lines 64-66), within the instant claimed range, about 0.1-49% or about 1-20% w/w, since converting the known actual amount by actual weight to weight percentage in a composition, w/w, is considered well within conventional skills in pharmaceutical science, involving merely routine skill in the art. The pharmaceutical composition of Nyce further comprises a preservative, an antioxidant, a flavoring agent (e.g., sugar, see col.7 line 10), a buffering agent, a dispersant, or a surfactant (see col.6 line 67 to col.8 line 1, and col.7 lines 33-38) an inert base, glycerol (glycerin, see col.7 line 11-12). Nyce also discloses the instant forms of the formulation, e.g., nasal (see col.7 line 17) oral, rectal, topical, transdermal, nasal, or parenteral including injectable (see col.5 lines 37-41, col.6 lines 40-67), in a solution (an aqueous liquor), suspension or

The cited prior art does not expressly disclose the particular particles of the active agents having respirable size herein.

Lieberman et al. teaches that a skilled artisan in pharmaceutical science would clearly knowledge that the granulation, determination of size, or size reduction of a solid pharmaceutical formulation, e.g., in nasal inhalation formulation, have several benefits, for example, as taught in a text book "Pharmaceutical Dosage Forms" Tables, (Volume 2) Ed. by Herbert A. Lieberman, Leon Leachman, and Joseph B. Schwartz (1989) at page 110. Moreover, suitable particle sizes for nasal inhalation are generally known and available to one of ordinary skill in the art.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation, since the nasal formulation or composition comprising two instant active agents is known based on Nyce. According to conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant is further requested to note that it is well settled that "intended use" of a composition or product, will not further limit claims drawn to a composition or product. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 165 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-19 of U.S. Patent No. 5,527,789 (of record).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent are drawn to a pharmaceutical composition comprising the dehydroepiandeosterone and ubiquinone with n being from 1 to 10, 6 to 10, or 10, and pharmaceutically acceptable carrier such as an aqueous or a solid carrier. The claim of the instant application is drawn to a pharmaceutical composition or formulation, or kit comprising the same dehydroepiandeosterone and ubiquinone with n being from 1 to 12, 1 to 10, 6 to 10, or 10, in the effective amounts, and pharmaceutically acceptable carrier such as an aqueous or a solid carrier, and this pharmaceutical composition or formulation, or kit may be further comprises other agents such as preservatives, antioxidants flavaoring agents, volatile oils, buffering agents, dispersants or surfactants.

Therefore, the claimed invention in claim 165 is clearly seen to be obvious over claims 13-19 of U.S. Patent No. 5,527,789.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is 571.272.0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on 571.272.0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
February 27, 2004